

CLAIMS

1. A process for producing a crystalline nucleus, wherein the crystalline nucleus is generated by irradiating a solution in which a solute to be
5 crystallized has dissolved, with at least one pulsed laser selected from a picosecond pulsed laser and a femtosecond pulsed laser.
2. The production process according to claim 1, wherein the crystalline nucleus is generated by focusing the pulsed laser in the solution with a lens
10 and causing a local explosion phenomenon once or more in a position on which the pulsed laser is focused.
3. The production process according to claim 1 or 2, wherein when the laser irradiation is carried out once, the pulsed laser has a pulse peak power
15 of at least 5×10^5 (watt).
4. The production process according to any one of claims 1 to 3, wherein when the laser irradiation is carried out once, the pulsed laser has a pulse energy of at least 60 nJ/pulse.
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5. The production process according to claim 1 or 2, wherein when the laser irradiation is carried out at 1000 pulses or more per second, the pulsed laser has a pulse peak power of at least 1×10^4 (watt).
- 25 6. The production process according to claim 1, 2, or 5, wherein when the laser irradiation is carried out at 1000 pulses or more per second, the pulsed laser has a pulse energy of at least 1.95 nJ/pulse.
7. The production process according to any one of claims 1 to 6, wherein
30 the pulsed laser is the femtosecond pulsed laser.
8. The production process according to any one of claims 1 to 7, wherein the number of times the solution is irradiated with the pulsed laser is a single shot to 10 million shots.
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9. The production process according to any one of claims 1 to 8, wherein the solution is a supersaturated solution.

10. A process for producing a crystal, wherein a crystalline nucleus is allowed to be generated in a solution by a process according to any one of claims 1 to 9 and then a crystal is grown thereon.
- 5 11. The production process according to claim 10, wherein a solute to be crystallized is an organic substance.
12. The production process according to claim 10, wherein a solute to be
10 crystallized is protein.
13. An apparatus for producing a crystalline nucleus that is used for carrying out a process according to any one of claims 1 to 9, wherein the apparatus comprises a pulsed laser irradiation means.
- 15 14. A method of screening crystallization conditions, comprising:
irradiating a solution in which a solute to be crystallized has dissolved, with at least one pulsed laser selected from a picosecond pulsed laser and a femtosecond pulsed laser; and
20 at least one of judging whether a crystalline nucleus has been generated by the laser irradiation and judging whether the solute has been altered by the laser irradiation.
15. The screening method according to claim 14, wherein a crystalline
25 nucleus is generated or denaturation of the solute is induced by focusing the pulsed laser in the solution with a lens and causing a local explosion phenomenon once or more in a position on which the pulsed laser is focused.
16. The screening method according to claim 14 or 15, wherein when the
30 laser irradiation is carried out once, the pulsed laser has a pulse peak power of at least 5×10^5 (watt).
17. The screening method according to any one of claims 14 to 16,
wherein when the laser irradiation is carried out once, the pulsed laser has a
35 pulse energy of at least 60 nJ/pulse.
18. The screening method according to claim 14 or 15, wherein when the

laser irradiation is carried out at 1000 pulses or more per second, the pulsed laser has a pulse peak power of at least 1×10^4 (watt).

19. The screening method according to claim 14, 15, or 18, wherein when
5 the laser irradiation is carried out at 1000 pulses or more per second, the pulsed laser has a pulse energy of at least 1.95 nJ/pulse.

20. The screening method according to any one of claims 14 to 19,
10 wherein the pulsed laser is the femtosecond pulsed laser.

21. The screening method according to any one of claims 14 to 20,
wherein the number of times the solution is irradiated with the pulsed laser is a single shot to 10 million shots.

22. The screening method according to any one of claims 14 to 21,
15 wherein the solution is a supersaturated solution.

23. The screening method according to any one of claims 14 to 22,
20 wherein the solute to be crystallized is an organic substance.

24. The screening method according to any one of claims 14 to 22,
wherein the solute to be crystallized is protein.

25. A screening apparatus for carrying out a screening method according
25 to any one of claims 14 to 24, wherein the apparatus comprises a pulsed laser irradiation means.

26. The production process according to claim 10, wherein a container
30 including the solution is allowed to make a movement to stir the solution and thereby the crystal is generated and grown.

27. The production process according to claim 26, wherein the movement
35 is a movement selected from rotation, vibration, and rocking or a movement in which two or more of them are combined together.

28. The production process according to claim 26 or 27, wherein the
container is a well plate including a plurality of wells, and each of the wells

contains the solution.

29. The production process according to any one of claims 26 to 28,
wherein the solution is brought into a supersaturation state by evaporating a
5 solvent contained in the solution or changing temperature of the solution.

30. The production process according to any one of claims 26 to 29,
wherein a liquid with a higher specific gravity than that of the solution is put
in the container, and the crystal is grown at an interface between the liquid
10 with a higher specific gravity and the solution.

31. The production process according to any one of claims 26 to 30,
wherein another container is prepared that contains a reservoir solution in
which components other than the solute of the solution have dissolved at
15 higher concentrations than in the solution, and then a crystal of the solute is
generated and grown in a state where water vapor can move between the
another container and the container including the solute.

32. The production process according to any one of claims 26 to 31,
20 wherein the solute of the solution is at least one selected from the group
consisting of resin, protein, saccharide, lipid, and nucleic acid.

33. A container that is used in a production process according to any one
of claims 1 to 12 or a container that is used in a screening method according
25 to any one of claims 14 to 24,

wherein the container comprises: a first chamber in which a solution
of a substance to be crystallized is put; a second chamber in which a reservoir
solution is put, in which only components other than the substance to be
crystallized of the solution of the substance to be crystallized have dissolved
30 at higher concentrations than in the solution of the substance to be
crystallized; and a passage that communicates with the first chamber and the
second chamber and allows gas to pass therethrough, and

a part or the whole of the first chamber is transparent or
semitransparent so as to allow the solution of the substance to be crystallized
35 to be irradiated with a laser beam.

34. The container according to claim 33, wherein the substance to be

crystallized is at least one selected from the group consisting of resin, protein, saccharide, lipid, and nucleic acid.

35. A plate that is used in a production process according to any one of
5 claims 1 to 12 or a plate that is used in a screening method according to any one of claims 14 to 24,

wherein the plate comprises a plurality of containers according to claim 33 formed therein.

10 36. The plate according to claim 35, wherein the substance to be crystallized is at least one selected from the group consisting of resin, protein, saccharide, lipid, and nucleic acid.

15 37. A container that is used in a production process according to any one of claims 1 to 12 or a container that is used in a screening method according to any one of claims 14 to 24,

wherein the container comprises: first chambers, in each of which a solution of a substance to be crystallized is put; a second chamber in which a reservoir solution is put, in which only components other than the substance
20 to be crystallized of the solution of the substance to be crystallized have dissolved at higher concentrations than in the solution of the substance to be crystallized; and passages that communicates with the first chambers and the second chamber and allow gas to pass therethrough,

the container includes a plurality of first chambers that communicate
25 with at least one second chamber through a plurality of passages,

the plurality of passages are different in at least one of diameter and length from each other, and

a part or the whole of the first chamber is transparent or semitransparent so as to allow the solution of the substance to be crystallized
30 to be irradiated with a laser beam.

38. The container according to claim 37, wherein the substance to be crystallized is at least one selected from the group consisting of resin, protein, saccharide, lipid, and nucleic acid.

35 39. A plate that is used in a production process according to any one of claims 1 to 12 or a plate that is used in a screening method according to any

one of claims 14 to 24,

wherein the plate comprises a plurality of containers according to claim 37 formed therein.

5 40. A container that is used in a production process according to any one of claims 1 to 12 or a container that is used in a screening method according to any one of claims 14 to 24,

wherein the container comprises: a first chamber in which a solution of a substance to be crystallized and an immiscible hyperbaric solution are
10 put, with the immiscible hyperbaric solution having a higher specific gravity than that of the solution of the substance to be crystallized and being immiscible with the solution of the substance to be crystallized; and a second chamber in which a reservoir solution is put, in which only components other than the substance to be crystallized of the solution of the substance to be
15 crystallized have dissolved at higher concentrations than in the solution of the substance to be crystallized,

the first chamber is formed in the second chamber,

the first chamber includes a large volume part in its lower portion and a small volume part in its upper part, with the small volume part having
20 a smaller volume than that of the large volume part,

an end of the upper part is open and gas can pass therethrough to move between the first and second chambers,

the solution of the substance to be crystallized is retained in at least the upper part of the first chamber or an opening part of the end, and

25 a part or the whole of the container is transparent or semitransparent so as to allow the solution of the substance to be crystallized to be subjected to laser irradiation.

41. The container according to claim 40, wherein in the first chamber, the
30 large volume part located in the lower part has a reverse truncated cone shape or a reverse truncated pyramid shape, the small volume part located in the upper part has a cylindrical shape or a rectangular-cylindrical shape, and the large volume part and the small volume part are joined to each other.

35 42. The container according to claim 41, wherein in the first chamber, a droplet of the solution of the substance to be crystallized is formed on the opening of the end of the small volume part located in the upper part, and in

this state, a solvent of the solution of the substance to be crystallized is evaporated.

43. The container according to any one of claims 40 to 42, wherein the
5 substance to be crystallized is at least one selected from the group consisting
of resin, protein, saccharide, lipid, and nucleic acid.

44. A plate that is used in a production process according to any one of
claims 1 to 12 or a plate that is used in a screening method according to any
10 one of claims 14 to 24,
wherein the plate comprises a plurality of containers according to
claim 40 formed therein.